

REMARKS

Status of the Claims

Claims 1-54 are pending. As is correctly stated in the Office Action, claims 2, 5, and 22-54 currently stand as being withdrawn from consideration. Claim 1 is canceled, above.

Restriction Requirement

A Restriction Requirement was mailed in connection with the instant application on March 8, 2004. As stated in the outstanding Office Action, Applicants elected Group 1 (claims 1, 3, 4, and 6-21) without traverse.

Issues under 35 U.S.C. § 112, First Paragraph

Claim 1 stands rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being adequately described in the Specification and/or having not been enabled by the Specification. This rejection is respectfully traversed. However, in view of the amendment, this rejection is moot.

Reconsideration and withdrawal of this rejection are requested.

Issues under 35 U.S.C. § 112, Second Paragraph

Claims 2 and 3 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite because the recitation of "a COX-2- selective substrate" is allegedly "not clear." This position is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Initially, Applicants point out that they believe that this rejection is intended to be directed to claim 1. Claim 2 is withdrawn, and claim 3 does not comprises the language at issue.

Nonetheless, a claim is definite within the meaning of 35 U.S.C. § 112, second paragraph, if it sets out and circumscribes a particular subject matter with a reasonable degree of clarity and particularly. See M.P.E.P. § 2173.02. Further, the Office is specifically instructed to “allow claims which define the patentable subject matter with a reasonable degree of particularly and distinctness. Id.

In the instant Application, “COX-2 selective substrate” is specifically defined in the “Definitions” section of the Specification beginning on page 9. For the convenience of the Examiner, a portion of that definition is reproduced below:

A COX-2 selective substrate is a substrate that is transformed to an enzymatic reaction product by the COX-2 enzyme; but is not transformed, or is not significantly transformed, to a reaction product by the COX-1 enzyme. ..

The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the Specification. “If the claims, when read in light of the Specification reasonable apprise those skilled in the art of the scope of the invention, § 112 demands no more.” *Miles Lab., Inc. v. Shandon, Inc.* 27 U.S.P.Q.2d 1123, 1126 (Fed. Cir. 1993).

Thus, this language clearly meets the legal standard for definiteness. One of ordinary skill in the art would understand the scope of the claims at issue to be clear. In short, if a substrate is transformed to an enzymatic reaction product by the COX-2 enzyme; but is not transformed, or is not significantly transformed, to a reaction product by the COX-1 enzyme, then the substrate is a COX-2 selective substrate of the present invention. If the substrate is transformed to an enzymatic reaction product by the COX-2 enzyme, and is also significantly transformed to a

reaction product by the COX-1 enzyme, then the substrate is not a COX-2 selective substrate of the present invention.

Further, the Specification provides examples of a "COX-2 selective substrate" of the present invention. For example, see page 10 (AEA).

Thus, notwithstanding the inapplicability of this rejection to claims 2 and 3, Applicants respectfully submit this the language at issues complies with 35 U.S.C. § 112.

Issues under 35 U.S.C. § 102

Claim 1 is rejected under 35 U.S.C. § 102(a), (b), and (e) as being allegedly anticipated by Isakson et al. (both WO 97/14679 (asserted under 102(b) and US 6,045,773 (asserted under 102 (a), (e)). These rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested. However, in view of the above amendment, this rejection is moot.

Claims 1, 3-4, 6-8, 10-17, and 19-21 are rejected under 35 U.S.C. § 102(b), as being allegedly anticipated by Yu et al. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested. Yu et al. describe the enzymatic conversion of arachidonyl ethanolaminde (anandamide, AEA) to PGE₂-ethanolamide in cell lines expressing COX-2, but not COX-1. See the specification at page 4. Also, see the Yu et al. abstract:

Incubation of anandamide with lysates and the intact cell line expressing COX-2 but not that of COX-1 produced prostaglandin E₂ ethanolamide. These results demonstrate the existence of a COX-2 mediated pathway for anandamide metabolism, and the metabolites formed represent a novel class of prostaglandins.

Yu et al. fail to disclose or suggest a method whereby direct detection of the claimed metabolites are indicative of an activity of a COX-2 enzyme. That is, Yu et al. fail to disclose or suggest the step of detecting a COX-2 specific metabolite, or detecting a metabolite of a COX-2 selective substrate to show COX-2 activity. Furthermore, Yu et al. fail to disclose or suggest a method whereby direct detection and quantification is indicative of an activity of a COX-2 enzyme.

Yu et al. measure relative initial rates of oxygenation of AA and AEA (Figure 1 of Yu) to determine COX activity against the substrate. With respect to the metabolites, Yu et al. disclose that COX-2 effectively oxygenated both AA and AEA as substrates (see p. 21184). Additionally, Yu et al. disclose that a metabolite of AEA is PGE₂ ethanolamide. However, Yu et al. fail to disclose or suggest the downstream metabolites of the present invention and, as stated above, the significance of their presence and quantification. Note the last paragraph of Yu et al., on page 21186: "At the present time the physiological significance of the metabolism of AEA by COX-2 is not known."

The present invention provides significant advantages over the prior art, such as the ability to detect and/or quantify COX-2 directly in the patient of sample thereof.

In order to anticipate a claim, each and every element as set forth in the claim must be described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Furthermore, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d

1913, 1920 (Fed. Cir. 1989). Applicants respectfully submit that in view of the deficiencies discussed above, it is clear that the references cited above do not anticipate the present invention.

In view of the above, Applicants respectfully request that the present rejection be withdrawn.

Issues under 35 U.S.C. § 103

Claims 9 and 18 are rejected under 35 U.S.C. § 103(a) as allegedly be obvious over Stichtenoth et al. and Yu et al. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The deficiencies of Yu et al. are discussed in detail, above. The Stichtenoth et al. article, as is indicated in the office action, fails to remedy the deficiencies of Yu et al. This reference is apparently asserted based solely on its disclosure of the use of urine as an assay sample.

Since the asserted references must, when combined, teach or suggest all of the claim limitations, the above combination does not present a *prima facie* case of obviousness.

In view of the above, Applicants respectfully request that this rejection be withdrawn.

Double Patenting Issues

Claim 1 is provisionally rejected based in the judicially created doctrine of double patenting. This rejection is respectfully traversed. However, in view of the above amendment, this rejection is moot.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants hereby petition for a two-month extension of time for filing a response to the outstanding Office Action. A Form PTO-2038 in the amount of \$225.00 for the extension of time fee is attached.

From the foregoing, further and favorable reconsideration in the form of a Notice of Allowability is requested and such action is believed to be in order.

If the Examiner has any questions concerning this amendment or the application in general, he is requested to contact the undersigned at the number listed below.

Respectfully submitted,



Richard S. Myers, Jr.
Registration No. 42,022
STITES & HARBISON
Customer No. 32885

Attorneys for Applicant
Telephone: (615) 782-2333